

Claims

1. A peptide characterised in that it

5 a) is at least 8 amino acids long and is a fragment of a mutant protein arising from a frameshift mutation in a gene of a cancer cell;

and

10 b) consists of at least one amino acid of the mutant part of a protein sequence encoded by said gene;

15 and

20 c) comprises 0-10 amino acids from the carboxyl terminus of the normal part of the protein sequence preceding the amino terminus of the mutant sequence and may further extend to the carboxyl terminus of the mutant part of the protein as determined by a new stop codon generated by the frameshift mutation;

25 and

30 d) induces, either in its full length or after processing by antigen presenting cell, T cell responses.

2. A peptide according to claim 1 characterised in that it contain 8-25 amino acids.

35 3. A peptide according to claim 1 characterised in that it contain 9-20 amino acids.

4. A peptide according to claim 1 characterised in that it contain 9-16 amino acids.

5. A peptide according to claim 1 characterised in that it 5 contain 8-12 amino acids.

6. A peptide according to claim 1 characterised in that it contain 20-25 amino acids.

10 7. A peptide according to claim 1 characterised in that it contains 9 amino acids.

8. A peptide according to claim 1 characterised in that it contains 12 amino acids.

15 9. A peptide according to claim 1 characterised in that it contains 13 amino acids.

10. A peptide according to claim 1 characterised in that it 20 is a fragment of a mutant protein encoded by a frameshift mutation in BAX gene or TGF β RII gene.

11. A peptide according to claim 1 characterised in that it is a fragment of a mutant protein encoded by a frameshift mutation in hTGF β 2 gene, DCC gene, BRCA1 gene, BRCA2 gene, hPTP gene, top2 gene, TTK gene, CTCF gene, Human FADD-homologous ICE/CED-3-like protease gene, hMSH3 gene, hRBP1 gene, hFMR1 gene, Human TINUR gene, b-raf oncogene, NF1 gene, Human germline n-myc gene, Human n-myc gene, Human ras inhibitor gene, hMSH6 gene, Human nasopharynx carcinoma EBV BNLF-1 gene, Human cell cycle regulatory protein (E1A-binding protein) p300 gene, bcl-3 gene, BIGH3, Human transcription factor ETV1 gene, IGFBP4 gene, Human MUC1 gene, JAK1 gene, JAK3 gene, Human Flt4 gene, Human p53 associated gene, hCAN gene, hDBL proto-oncogene/hMCF2PO gene, hDEK gene, p107 gene, hGPR1 gene, hRBP56 gene, hITF-2 gene, hKiSS-1 gene, hTP-1 gene, hFDF-5 gene, hMTA1 gene, hTFIIB90 gene, hLUCA-1 gene, Human Wilm's tumour (WIT-1) associated protein, ICErel-III gene, FasL gene, BARD1 gene, hMCF.2 gene, fas gene and Human DPC4 gene.

12. A peptide according to claim 1 characterised in that it is selected from a group of peptides having the following sequence identity numbers:
seq. id. nos. 1-21, seq. id. no. 428, seq. id. no. 438 and seq. id. nos. 456-458 or a fragment of any of these.

13. A peptide according to claim 1 characterised in that it is selected from a group of peptides having the following sequence identity numbers:
seq. id. nos. 22-427, seq. id. nos. 429-437, seq. id. nos. 439-455 and seq. id. no. 459 or a fragment of any of these.

14. A pharmaceutical composition comprising a peptide according to any of the above claims and a pharmaceutically acceptable carrier or diluent.

15. A cancer vaccine comprising a peptide according to any of the claims 1-13 and a pharmaceutically acceptable carrier or diluent.

5 16. Use of a peptide according to any of the claims 1-13 for the preparation of a pharmaceutical composition for treatment or prophylaxis of cancer.

10 17. Method for vaccination of a person disposed for or afflicted with cancer, consisting of administering at least one peptide according to the claims 1-13, one or more times, in an amount sufficient for induction of specific T-cell immunity to the mutant proteins or fragments thereof encoded by a frameshift mutated gene.

15 18. Method according to claim 17 wherein the amount of the peptides is in the range of 1 microgram (1 μ g) to 1 gram (1g) and preferentially in the range of 1 microgram (1 μ g) to 1 milligram (1 mg) for each administration.

20 19. Method for treatment of a patient afflicted with cancer by stimulating in vivo or ex vivo with peptides according to the claims 1-13.

25 20. Method according to claim 19 wherein the amount of the peptides used is in the range of 1 microgram (1 μ g) to 1 gram (1g) and preferentially in the range of 1 microgram (1 μ g) to 1 milligram (1 mg) for each administration.

30 21. A pharmaceutical composition or vaccine composition comprising a combination of at least one peptide according to claims 1-13 and at least one peptide according to PCT/NO92/00032.

22. A method for identifying new peptides which correspond to fragments of proteins arising from frameshift mutations in genes, characterised by the following steps:

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1) identifying a gene in a cancer cell susceptible to frameshift mutation by having a mono nucleoside base repeat sequence of at least five residues, or a di-nucleoside base repeat sequence of at least four di-nucleoside base units;

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and

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2) removing, respectively, one nucleoside base residue or one di-nucleoside base unit from the repeat sequence and identifying the amino acid sequence of the protein encoded by the altered gene sequence as far as to include a new stop codon;

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and/or

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3) removing, respectively, two nucleoside base residues or two di-nucleoside base units from the repeat sequence and identifying the amino acid sequence of the protein encoded by the altered gene sequence as far as to include a new stop codon;

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and/or

4) inserting, respectively, one nucleoside base residue or one di-nucleoside base unit in the repeat sequence and identifying the amino acid sequence of the protein encoded by the altered gene sequence as far as to include a new stop codon;

35

and/or

5) inserting, respectively, two nucleoside base residues or two di-nucleoside base units in the repeat sequence and identifying the amino acid sequence of the protein encoded by the altered gene sequence as far as to include a new stop codon.

23. A method according to claim 22,
10 charactersed it that it includes the following steps:

15 6) determining whether the new peptides, either in their full length or as shorter fragments of the peptides, are able to stimulate T cells;

and optionally

20 7) determining peptides containing nested epitopes for different major HLA class I and/or HLA class II molecules.

24. An isolated DNA sequence comprising a DNA sequence or variants thereof encoding a frameshift mutant peptide
25 according to claim 1.

25. An isolated DNA sequence encoding peptides comprising seq. id. nos. 1-21, seq. id. no. 428, seq. id. no. 438 and seq. id. nos. 456-458 or variants thereof.

30 26. An isolated DNA sequence encoding peptides comprising seq. id. nos. 22-427, seq. id. nos. 429-437, seq. id. nos. 439-455 and seq. id. no. 459 or variants thereof.

27. Use of a DNA sequence according to any of the claims 24-26 for the preparation of a pharmaceutical composition for treatment or prophylaxis of cancer.

5 28. Method for treatment of a person disposed for or afflicted with cancer, by stimulating *in vivo* or *ex vivo* with DNA sequences according to the claims 24-26.

10 29. A plasmid or virus vector comprising the DNA sequence of claim 24 encoding a frameshift mutant peptide.

15 30. A vector according to claim 29 wherein the vector is *E.Coli* plasmid, a *Listeria* vector and recombinant viral vectors. Recombinant viral vectors include, but are not limited to orthopox virus, canary virus, capripox virus, suipox virus, vaccinia, baculovirus, human adenovirus, SV40 or bovine papilloma virus.

20 31. Use of a plasmid or virus vector according to claim 29 for the preparation of a pharmaceutical composition for treatment or prophylaxis of cancer.

25 32. Method for treatment of a person disposed for or afflicted with cancer, by stimulating *in vivo* or *ex vivo* with plasmids or virus vectors according to claim 29.